AN IN-VITRO COMPARISON OF DRUG DEPOSITION FROM A COMMERCIALLY AVAILABLE DRY POWDER INHALER AND A PRESSURISED AEROSOL PACK

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Drugs administered with metered dose inhalers (MDI) are prone to "inhalation errors" because many patients are incapable of co-ordinating the activation of the aerosol with inspiration. However up to 95% of these subjects can use a dry powder device (DPD) without difficulty (Paterson & Crompton 1976). Clinical evaluation of DPDs has shown that in general bioequivalence with MDIs is only achieved by using a higher dose. In this study the distribution of salbutamol sulphate (Rotocap®), from a commercially available DPD (Rotahaler®) was examined in an *in vitro* model lung and compared with the distribution of salbutamol base from a MDI (Ventolin®). Previous work of this type has been reported only for an earlier design of Rotahaler (Hallworth 1977).

The model lung has been described previously (Lam et al 1984) and is designed to measure size distribution and deposition over realistic time intervals. The essential features consist of a glass "mouth" and "trachea" connected to two "primary bronchi". Air is drawn through each bronchus at a flow rate of 28.3 l min^{-1} which accommodates the operational flow rate of an Andersen sampler (connected in line on one bronchus) yet gives a combined air flow at the mouthpiece of 56.5 l min^{-1} commensurate with a "normal" inspiration rate. Five 400 µg Rotacaps were broken within the Rotahaler in the manner prescribed by the manufacturer. The DPD was then discharged by rerouting the airstream instantaneously from around the Rotahaler to through it. The MDI was discharged 20 times into the model upper airway, allowing 5 second intervals between each activation.

Table Summary of deposition characterisitcs of the MDI and DPD

Device	% Total Dose Recovered (n=6)	% Dose Less than 5 µm (n=6)	Weight of salbutamol deposited below 5 µm
DPD	104±8	25.77±0.67	108±3 µg
MDI	96±16	61.30±15.08	118±20 µg

The salbutamol sulphate from the DPD was found to be evenly distributed throughout the stages of the Andersen sampler. Electron microscopy showed that most of the crystalline lactose used as dilutent was deposited on the upper portion of the model. Particles with an aerodynamic diameter of less than 5 µm (plates 3-7 of the sampler) are generally accepted as being the most useful therapeutically. The DPD and MDI respectively gave 108±3 and 118±20 µg of drug (calculated as equivalent base for the sulphate) in this size range from their respective unit doses (400 µg Rotacap , 200 µg activation of Ventolin). On this basis the *in vitro* model lung system would appear to provide a means by which aerosol formulations can be both developed and optimised.

These results show that deposition from the DPD can be considered inefficient when compared to the MDI in terms of the percentage dose deposited within the therapeutic size range. However one 400 µg capsule can be seen to provide a similar level of medication to the 200 µg unit dose from an MDI, since the amount of drug deposited having an aerodynamic diameter of less than 5 µm is comparable. These results support clinical studies which showed no significant differences in bronchodilation responses between salbutamol at these concentrations from the two dosage forms (Hartley et al 1977).

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